SUSCEPTIBILITY TO UV RADIATION-INDUCED SUPPRESSION OF IMMUNE RESPONSES & THE RELATIONSHIP TO ENHANCED RISK OF INFECTIOUS DISEASE.

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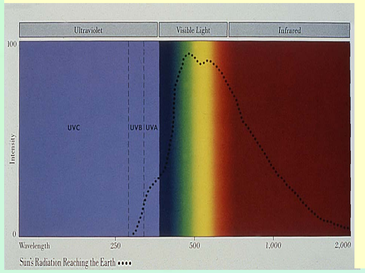
Sensitive Sub-Populations

The Environmental Issue

- The stratospheric ozone layer prevents penetration of ultraviolet radiation from the sun to the earth's surface
- Chlorofluorocarbons (CFC's) such as freon damage the ozone layer shifting the curve below to the left and increasing human exposure to UVR



- UVR increases the risk of skin cancer & cataracts, risk is based on cumulative exposure
- UVR suppresses immune responses that are important defenses against infectious disease & tumors, and are important for vaccine effectiveness; effects are seen following acute exposure

- A dose response is needed for UVR-induced immune suppression in order to predict increased risk from stratospheric ozone depletion.
- Pigmentation protects against UV-induced skin tumors

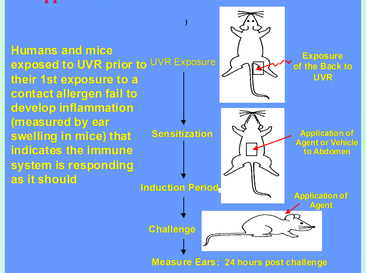
OBJECTIVES OF THESE STUDIES

- Determine whether pigmentation protects against UVR-induced immune suppression
- Develop a biologically-based dose response in humans for UVR-induced immune suppression
- Assess the value of mouse studies in predicting human effects
- Determine the relationship between UVR-induced immune suppression and enhanced susceptibility to infectious disease.

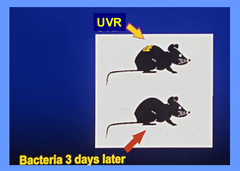
Scientific Approach

- **185 human subjects with varying degrees of pigmentation were exposed to UVR and immune function tests were performed.**

Contact sensitivity was used to assess immune responses in humans and in strains of mice with different sensitivity to UVR-induced immune suppression.



Mice were also exposed to UVR and challenged with the vaccine strain of tuberculosis

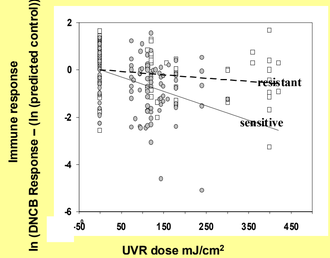


Immune responses to subsequent challege with tuberculin antigen, and numbers of bacteria in spleen and lymph node were assessed

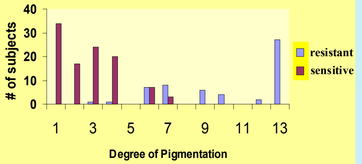
Results

Results from Human Subject Studies

- Pigmentation did not contribute significantly to differences in sensitivity to UVR-induced immune suppression (5 different skin types were studied)
- Subjects could be divided into 2 groups, sensitive to immune suppression and resistant based on the vigor of their erythemal (sun burn) response to UVR
- Those with steep dose responses for sunburn (including some people of color) were sensitive; those with moderate or flat sun burn responses were resistant



Sensitive individuals included people of color



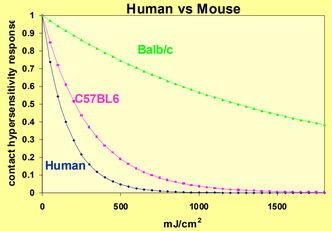
The dose of UVR required to suppress the immune response in sensitive subjects by 50%, was 113.6 mJ/cm² with a 95% confidence interval of (68.7, 170.3) or approximately 2 minimal erythemal (sun burn) dose (MED)

Similar Responses for most sensitive mouse strain & sensitive human subjects

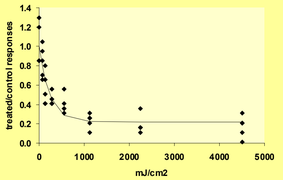
Species (Strain)	Local[b] 50% suppression dose mJ/cm²	Local[b] 10% suppression dose mJ/cm²	Systemic[c] 50% suppression dose mJ/cm²	Systemic[c] 10% suppression dose mJ/cm²
Mouse (BALB/c)	1246	177	1137	130
Mouse (C57BL/6)	210	32	220	33
Human	114 (69,170)[d]	17 (-55, 62)[d]	ND[e]	ND

[a]Mouse data from Noonan and De Fabo, 1990; Human data from Selgrade et al, 2001.
[b]Contact sensitizer applied at the site of irradiation
[c]Contact sensitizer applied at a site distant from the irradiation site
[d]confidence interval
[e]not done

Immune Suppression Dose Response Human vs Mouse



UV suppressed immune response to tuberculosis vaccine



Impact

- Risk assessors have a biologically based dose response for an acute effect of UVR exposure
- Data can be used to assess the public health impact of U.S. participation in the Montreal Treaty to phase our chlorofluoro carbons
- Provides a rationale for extrapolating from suppression of immune responses enhanced susceptibility to disease
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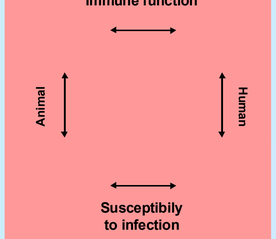

Building the scientific foundation for sound environmental decisions